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NOV 14 1983

Sandoz, Inc.
Pharmaceutical Division
Drug Registration & Regulatory Affairs
Attention: Richard J. Raffa
Senior Project Coordination Manager
East Hanover, New Jersey 07936

Dear Mr. Raffa:

Reference is made to your Antibiotic Form 5 Applications dated November 12, 1982, submitted pursuant to Section 507 of the Federal Food, Drug and Cosmetic Act for the preparations SANDIMUNE (cyclosporine) concentrate for infusion and oral solution.

We also refer to your submissions of April 22, July 29, September 7 and 9, October 13, and December 29, 1982, and January 20, February 15, March 2, 7, 11 and 30, April 20 and 27, May 4 and 9, June 1, 6, 7 and 27, September 23, October 5 and 19, and November 7, 1983.

The application was filed on November 7, 1983.

We have completed the review of these applications as amended and have concluded that the drug is safe and effective for use as recommended in your draft labeling submitted November 7, 1983, and modified below. Accordingly, the applications are approved.

In the WARNINGS section of your draft package insert, the paragraph on lymphomas should be deleted and the following statement substituted for it:

"Lymphomas have developed in patients receiving cyclosporine and other forms of immunosuppressive therapy after transplantation though no causal relationship has been established. With cyclosporine some patients have developed a lymphoproliferative disorder which regresses when the drug is discontinued."

In the ADVERSE REACTIONS section, in the table on page nine, "Renal Transplant Patients in Whom Therapy Was Discontinued," under "Reason for Discontinuation," "Lymphoma" should be changed to "Lymphoma/Lymphoproliferative Disease."

"A Practical Guide," included in your promotional material, contains on page fourteen under "Administration" a comment about using a glass container and rinsing it with additional diluent to ensure that the total dose is taken. This information should be added to the DOSAGE AND ADMINISTRATION section, Sandimmune Oral Solution subsection.

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The DESCRIPTION and HOW SUPPLIED sections should be revised as discussed in the telephone conversation between yourself and Ms. Lee Ripper of this Administration on November 10, 1983.

The final printed labeling should include the above revisions, but otherwise be identical in content to the draft copy. Please submit twelve copies of the printed labeling to each application.

The enclosures summarize the conditions related to the approval of these applications.

The following expiries are approved:

24 months for the concentration for infusion (5 ml sterile ampule containing 50 mg cyclosporine per ml).

24 months for the oral solution (50 ml bottle containing 100 mg cyclosporine per ml).

Please submit one market package of each preparation of the drug when available.

We await submission of the results of your Phase IV bioavailability study as committed to in your letter of September 23, 1983.

Sincerely yours,

RT

Robert J. Temple, M.D.
Acting Director
Office of Drug Research and Review
National Center for Drugs and Biologics

Enclosure

Records and Reports Requirements
(Reg. 431.60-431.62)